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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)	
133172.02201	

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to "Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)]

on _____

Signature _____

Typed or printed name _____

Application Number	Filed
10518701	September 1, 2005

First Named Inventor: Arnold I. Levinson

Art Unit	Examiner
1644	Michael E. Szperka

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☑ attorney or agent of record. Registration number 52,201
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

/Daniel M. Scolnick, Reg. No. 52,201/
Signature

Daniel M. Scolnick
Typed or printed name

610-640-7820
Telephone number

July 23, 2009
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Arnold I. Levinson *et al.*
Serial No.: 10/518,701
Filed: September 1, 2005
Group Art Unit: 1644
Examiner: Michael E. Szperka
Confirmation No.: 5645

Title: VACCINES FOR SUPPRESSING IGE-MEDIATED ALLERGIC DISEASE AND METHODS FOR USING THE SAME

Mail Stop: AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Pre-Appeal Brief Request for Review

Dear Sir:

In response to the Final Rejection dated January 23, 2009 and the Advisory Action dated April 7, 2009, Applicants respectfully request reconsideration of the pending rejections.

I. Claims 1-3, 5-7, 22-24, and 26-29 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chen *et al.* (WO 98/53843) in view of Wang *et al.* (WO 99/67293) in view of Hollis *et al.* (U.S. Patent No. 5,629,415) and in view of Rutter (U.S. Patent No. 4,769,326). The Office alleges that the Chen reference discloses vaccine constructs comprising the membrane bound domain of IgE coupled to heterologous sequences including helper T epitopes. The Office acknowledges that the Chen reference fails to disclose a composition with a proteolytic cleavage sequence. The Office alleges the deficiency is remedied by the Rutter reference which allegedly discloses the use of linkers comprising proteolytic cleavage sites because the linkers "allow for efficient incorporation and removal of desired functional properties." (Final Office Action p. 5). Applicants respectfully disagree.

The office has clearly erred by not properly establishing a *prima facie* case of obviousness and because the cited references teach away from the claimed invention. The Chen and Wang references teach away from using a proteolytic cleavage sequence, which would allow the components of the construct to be unconjugated. One of skill in the art reading the Chen and Wang references would be led to use a composition that conjugates the two components without the two components being able to be cleaved. For example, the Chen reference repeatedly describes conjugates and does not state that the conjugated composition can include a cleavage

sequence. Additionally, the Chen reference states that for conjugates in human use one would expect that there would be "no inhibition of IgE responses to unrelated, ***unconjugated*** antigens." (Chen, p. 10, line 22, emphasis added.). "'A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.'" *Optivus Tech., Inc. v. Ion Beam Applications S.A.*, 469 F.3d 978, 989 (Fed. Cir. 2006) (quoting *In re Kahn*, 441 F.3d 977, 990 (Fed. Cir. 2006)). Here, the Chen reference teaches away because it states that there would be no inhibition of IgE responses for unconjugated antigens. Therefore, one of skill in the art reading the Chen reference in its entirety would not have inserted a proteolytic cleavage sequence because such a construct would lead to an unconjugated composition leading to a result that is not desired. Accordingly, the Chen reference teaches away from using a construct that would allow the epitopes to be separated by use of a cleavage sequence.

The Wang reference also teaches away from including a proteolytic cleavage sequence. The Wang reference discloses the use of a spacer between its components and states that the two components are "adjacent to either the N- or C-terminus of IgE-CH3 domain antigen sequences, ***in order to evoke efficient*** antibody responses." (Wang, p. 28-29). Like the Chen reference, the Wang reference teaches that the components should be next to one another and linked so that there is a proper response. The Wang reference fails to suggest decoupling the components and teaches away from such a method because it would not "evoke [an] efficient antibody response[]."

The Advisory Action argues that the proteolytic cleavage sequence may not be cleaved *in vivo* and that separation is not a limitation of the claim. The Office's assertion is reading the limitation out of the claim. The cleavage sequence is a functional cleavage sequence otherwise the term cleavage sequence would have no meaning. One of skill in the art reading the references would not have added a cleavage sequence because the purpose of including a cleavage sequence is to allow the parts to be separated, which is exactly what the references teach away from. Accordingly, one of skill in the art would not have used a proteolytic cleavage sequence because the Wang and Chen references teach away from allowing the components to be separated. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

II. Claims 1-3, 5-7, 22-24, and 26-29 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Klysner *et al.* (WO 02/20038) in view of Wang *et al.* (WO 99/67293) and in view of Rutter. Claims 1-3, 5-7, 22-24, and 26-29 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Klysner *et al.* (US 2002/0172673) in view of Wang *et al.* (WO 99/67293) and in view of Rutter. The Office acknowledges that the Klysner reference fails to disclose the use of linkers comprising a proteolytic cleavage sequence between the epitopes. (Office Action, page 6). The Office alleges that the Rutter reference cures this deficiency. Applicants respectfully disagree.

The Office has clearly erred because the claims are not obvious because the Klysner and Wang references each teach away from inserting a proteolytic cleavage sequence. The Wang reference teaches away for the reasons stated above. The Klysner reference also teaches away because the Klysner reference teaches that the epitopes described in Klysner should be simultaneously presented by the antigen presenting cells. (Klysner, p. 13, lines 14-20)[1]. The inclusion of a proteolytic cleavage sequence that allows the epitopes to be separated would function to reduce the likelihood of simultaneous presentation of the epitopes by the antigen presenting cells. One of skill in the art would not have been led to insert a proteolytic cleavage sequence because it would be contrary to what the Klysner reference states is necessary for an effective use, that is the simultaneous presentation of the epitopes by the antigen presenting cells. Thus, the Klysner reference teaches away from using a proteolytic cleavage sequence.

The Advisory Action argues that the proteolytic cleavage sequence may not be cleaved *in vivo* and that separation is not a limitation of the claim. The Office's assertion is reading the limitation out of the claim. The cleavage sequence is a functional cleavage sequence otherwise the term cleavage sequence would have no meaning. One of skill in the art reading the references would not have added a cleavage sequence because the purpose of including a cleavage sequence is to allow the parts to be separated, which is exactly what the references teach away from. Accordingly, one of skill in the art would not have used a proteolytic cleavage sequence because the Klysner and Wang references teach away from allowing the components to be separated, and, therefore, the references teach away from including a cleavage sequence.

[1] Applicants note that the two Klysner references are the same. Page and line number refer to WO 02/20038

Therefore, the claims are not obvious because the Klysner and Wang references teach away and because the combination of the references would not have suggested one of skill in the art to insert a proteolytic cleavage sequence. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

III. Claims 8, 32-37, 50, 58-73 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Chen et al (WO 98/53843) in view of Wang et al. (WO 96/67293) in view of Hollis et al. (U.S. Patent No. 5,629,415) and in view of Rutter (U.S. Patent 4,769,326) as applied to claims 1-3, 5-7, 22-24, and 26-29, and further in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929) as evidenced by Janeway et al (Immunobiology, 3rd Edition, Garland Publications, 1997, pages 3:26-3:31). Claims 8, 32-37, 50, 58-73 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Klysner (WO 02/20038) in view of Wang et al. (WO 96/67293) in view of Hollis et al. (U.S. Patent No. 5,629,415) and in view of Rutter (U.S. Patent 4,769,326) as applied to claims 1-3, 5-7, 22-24, and 26-29, and further in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929) as evidenced by Janeway et al (Immunobiology, 3rd Edition, Garland Publications, 1997, pages 3:26-3:31). Claims 8, 32-37, 50, 58-73 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Klysner (US 2002/0172673) in view of Wang et al. (WO 96/67293) in view of Hollis et al. (U.S. Patent No. 5,629,415) and in view of Rutter (U.S. Patent 4,769,326) as applied to claims 1-3, 5-7, 22-24, and 26-29, and further in view of Walls et al. (Nucleic Acids Research, 1993, 21:2921-2929) as evidenced by Janeway et al (Immunobiology, 3rd Edition, Garland Publications, 1997, pages 3:26-3:31). Applicants respectfully disagree and assert that the Office has clearly erred because the combination fails to yield the claimed invention.

The Office alleges that the combination of references discloses each and every element of claims 8, 32-37, 50, 58-73. In support of this contention the Office states:

> Note that as evidenced by Janeway et al., immunoglobulin genes are assembled via the process of V(D)J recombination, and that different isotypes (i.e. IgG, IgE, IgA) are obtained by isotype switching. As such the immunoglobulin heavy chain leader sequence is upstream of the rearranged variable domain . . . and thus an "IgE leader" is the ***same sequence*** as an IgM, IgD, IgG, and IgA leader sequence...Thus, the "Ig leader" of Walls *et al.* is an "IgE leader."

(Final Office Action, pages 9-10, emphasis added). Applicants previously submitted a declaration pursuant to 37 C.F.R. § 1.132 by Dr. David B. Weiner. The declaration lists the amino acid leader sequences from sequences that have been labeled as IgE variable, IgA constant, IgA, variable 1, IgA variable 2, IgA variable 3, IgG constant, IgM variable, and IgM VH1. The declaration also shows the sequence similarity between the different leader sequences. The declaration shows that the IgE leader sequence is not 100% identical to the other leader sequences. The declaration states, "[t]he alignments show that IgE leader sequence is not the same as the leader sequences from the different isotypes." (Declaration, ¶ 3). Therefore, the "Ig leader" of the Walls reference is not an "IgE leader." Therefore, the Office has failed to present a proper *prima facie* obviousness rejection because even if all the references were combined the combination does not yield the present invention.

The Office has rejected the Declaration because of the apparent lack of Genbank or other source identifiers. The Declaration must be treated as a fact and as such Applicant has provided evidence showing that not all leader sequences are the same. The Office has not provided any evidence to show that the facts presented in the declaration are incorrect. The sequences demonstrate that not all leader sequences are the same, and, therefore, the rejection is improper for the reasons stated above.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn

Applicants respectfully submit that the claims are in condition for allowance. The Office is invited to contact Applicants' undersigned representative at 610-640-7820 to resolve any remaining issues. The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully Submitted,
/Daniel M. Scolnick, Reg. No. 52,201/
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Registration No. 52,201

Dated: **July 23, 2009**
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